UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,476	09/30/2003	Robert B. DuBridge	181 US UT01	7526

47470 7590 05/17/2007

PDL BIOPHARMA, INC.
Attn: Legal Department
34801 CAMPUS DRIVE
FREMONT, CA 94555

EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	
MAIL DATE	**DELIVERY MODE**
05/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/676,476	DUBRIDGE, ROBERT B.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment, filed 2/15/2007, in which claims 1-65 were canceled, claims 66, 69 and 70 were amended, and claims 84-88 were newly added. Currently, claims 66-88 are pending.

Applicant's arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

Election/Restrictions

Applicant elected Group I without traverse in the reply filed 3/18/2005. Applicant confirmed the provisional election of Flp recombinase as the species of recombinase in the reply filed 11/29/2005. All pending claims are readable upon the elected invention.

Currently, claims 66-88 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 85-88 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This is a new rejection, necessitated by the addition of new claims 85-88 in the reply filed 2/15/2007.

Claim 85 is vague and indefinite in that the metes and bounds of the phrase "in which the first target element further comprises a first target gene and a first scorable marker gene encoding cell surface protein" are unclear. The phrase is unclear in that claim 85 depends from claim 73, which requires the presence of a first target gene and a first selectable marker gene. It is unclear if the first target element further comprises another target gene and another scorable marker gene, which is a cell surface protein. Alternatively, the phrase could be interpreted as limiting the first marker gene, recited in claim 73, to a cell surface protein. It would be remedial to amend the claim language to clearly indicate that claim 85 limits the first selectable marker gene of the first target element to a cell surface protein (e.g. wherein the first selectable marker gene of the first target element is a cell surface protein).

Claim 86 depends from claim 85 and thus is indefinite for the same reasons applied to claim 85.

Claim 87 is vague and indefinite in that the metes and bounds of the phrase "in which the second target element further comprises a second target gene and a second selectable marker gene encoding a cell surface protein" are unclear. The phrase is unclear in that claim 87 depends from claim 78, which requires the second target element to comprise a second target gene and a second selectable marker. It is unclear if the second target gene further comprises another target gene and another selectable marker, which is a cell surface protein. Alternatively, the phrase could be interpreted as limiting the second marker gene, recited in claim 78, to a cell surface protein. It would be remedial to amend the claim language to clearly indicate that claim 87 limits the second marker gene of the second target element to a cell surface protein (e.g. wherein the second marker gene of the second target element is a cell surface protein).

Claim 88 depends from claim 87 and is thus indefinite for the same reasons applied to claim 87.

Response to Arguments - 35 USC § 112

As noted on pages 7-8 of the reply filed 2/15/2007, claims 69 and 70 should have been rejected under 35 U.S.C. 112, second paragraph, for the reasons applied to canceled claim 5 in the prior action. The rejection under 35 U.S.C. 112, second paragraph, has been withdrawn in view of Applicant's amendment to the claims (claims 69 and 70) in the reply filed 2/15/2007 such that the claims conform to accepted Markush-type language.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 66 and 69-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheo et al (US Patent Application Publication No. 2002/0007051, cited in a prior action; see the entire reference) in view of Seibler et al (Biochemistry, Vol. 36, pages 1740-1747, 1997, cited in a prior action; see the entire reference) and Mazda et al (Journal of Immunological Methods, Vol. 169, pages 53-61, 1994; see the entire reference). This is a new rejection, necessitated by

the amendment of claim 66 to limit the first scorable homeostatic reporter element to one that comprises a scorable reporter gene encoding CD8, in the reply filed 2/15/2007.

Regarding claim 66, Cheo et al teach an integration cassette (e.g. starting molecule or Destination vector) comprising two recombination sites flanking promoters, selectable markers, and tags such histidine tags or green fluorescent protein (e.g. paragraphs [0045], [0050], [0147], [0148], [208] and [0488]; Figure 6). Cheo et al define the term "selectable marker" to mean a nucleic acid segment that allows one to select for or against a molecule or cell that contains it, often under particular conditions, including nucleic acid segments that encode products which can be readily identified (e.g., phenotypic markers such as P-galactosidase, green fluorescent protein (GFP), yellow fluorescent protein (YFP), red fluorescent protein (RFP), cyan fluorescent protein (CFP), and cell surface proteins (paragraph [0258]). Further, Cheo et al teach the addition of regions that allow integration into eukaryotic chromosomes (e.g. transposable elements) (e.g. paragraph [0327]). As a general rule, the insertion of transposons into target DNA is a random event (e.g. paragraph [0010]). Cheo et al teach a first target cassette comprising a polynucleotide to be substituted into the integration cassette flanked by two recombination sites (e.g. paragraphs [0045] and [0075]). Regarding the recombination sites and additional vectors, Cheo et al teach the following:

> In another specific aspect, the invention provides a method of cloning comprising providing at least a first nucleic acid molecule comprising at least a first and a second recombination site and at least a second nucleic acid molecule comprising at least a third and a fourth recombination site, wherein none of the first, second, third or fourth recombination sites is capable of recombining with any of the other sites, providing one or more vectors (e.g., two, three, four, five, seven, ten, twelve, etc.), comprising at least a fifth, sixth, seventh and eighth recombination site, wherein each of the fifth, sixth, seventh and eighth recombination sites are capable of recombining with one of the first, second, third or fourth recombination site, and conducting a recombination reaction such that at

least said first and second molecules are recombined into said vectors. See paragraph [0154].

See also Figures 6 and 7 and paragraph [0075], for example. Further, Cheo et al teach a recombinase activity capable of recognizing the recombinase recognition sites of the second integration cassette and second target cassette (e.g. paragraphs [0055], [0196], [0253] and [0295]). Cheo et al teach the use of the Flp recombinase protein to catalyze recombination between Frt sites (e.g. paragraphs [0047], [0048], [0055] and [0253]).

Regarding claim 69, Cheo et al teach the use of makers that are the same or different, where the markers encode a cell surface protein (e.g. paragraphs [0046], [0148] and [0258]).

Regarding claim 70, Cheo et al teach the use of mammalian cells, yeast cells and bacterial cells (e.g. paragraph [0436]). Thus, the integration cassette would be capable of integrating in mammalian, yeast or bacterial cells.

Regarding claim 71, Cheo et al teach the use of a first integration cassette comprising two, three, four etc. open reading frames that further comprise sequences that function as internal ribosome entry sites (IRES) (e.g. paragraph [0147]). The IRES allows the expression of two structural genes from a single transcript (i.e. bi-cistronic element) (e.g. paragraph [0544]).

Regarding claim 72, Cheo et al teach the use of a first integration cassette comprising a gene encoding a fusion protein comprising an N- or C-terminal tag such as an epitope tag or a six histidine tag (e.g. paragraph [0062]).

Regarding claim 73, Cheo et al teach a first target cassette comprising a first target gene and a first selectable marker gene that may be the same or different marker as compared to a selectable marker in the first integration cassette (e.g. paragraphs [0046] and [0148]).

Regarding claim 74, Cheo et al teach a first target cassette further comprising a plolycistronic element by including an IRES sequence to permit the bi-cistronic expression of two gene products from a single promoter (e.g. paragraphs [0143] and [0544]).

Regarding claim 75, Cheo et al teach the use of tagged proteins such as his tags (e.g. paragraph [0034]).

Regarding claim 76, Cheo et al teach a second integration cassette comprising a gene encoding a fusion protein comprising an N- or C-terminal tag such as an epitope tag or a six histidine tag (e.g. paragraph [0062]).

Regarding claim 77, Cheo et al teach a second integration cassette comprising two, three, four etc. open reading frames that further comprise sequences that function as internal ribosome entry sites (IRES) (e.g. paragraph [0147]). The IRES allows the expression of two structural genes from a single transcript (i.e. bi-cistronic element) (e.g. paragraph [0544]).

Regarding claim 78, Cheo et al teach a second target cassette comprising a first target gene and a first selectable marker gene that may be the same or different marker as compared to a selectable marker in the second integration cassette (e.g. paragraphs [0046] and [0148]).

Regarding claim 79, Cheo et al teach a second target cassette further comprising a plolycistronic element by including an IRES sequence to permit the bi-cistronic expression of two gene products from a single promoter (e.g. paragraphs [0143] and [0544]).

Regarding claim 80, Cheo et al teach the use of tagged proteins such as his tags (e.g. paragraph [0034]).

Regarding claim 81, Cheo et al teach the use of the system of claim 66 (described above) with nucleic acid molecules encoding more than one subunit of a multi-subunit complex such as an enzyme (e.g. paragraphs [0168] and [0354]).

Regarding claim 82, Cheo et al teach the use of the system of claim 66 (described above) with nucleic acid molecules encoding a multi-subunit complex that comprises an antibody molecule (e.g. paragraph [0168]).

Regarding claim 83, the recombination sites of the vectors function as "cloning sites" to clone recombinant molecules. Further, Cheo et al teach the inclusion of one or more restriction sites (e.g. multiple cloning sites) in the nucleic acid cassettes of the invention (e.g. paragraph [0140]).

Regarding claim 85, the claim has been interpreted as limiting the first scorable marker gene of the first target element to a cell surface protein. Cheo et al teach the use of makers that are the same or different, where the markers encode a cell surface protein (e.g. paragraphs [0046], [0148] and [0258]).

Regarding claim 87, the claim has been interpreted as limiting the selectable marker gene of the second target element to a cell surface marker. Cheo et al teach the use of makers that are the same or different, where the markers encode a cell surface protein (e.g. paragraphs [0046], [0148] and [0258]).

Cheo et al do not teach a rec element encoding at least one flp recombinase activity that recognizes the recombinase recognition sites of the first integration cassette and second integration cassette. Cheo et al do not teach the use of maker genes that encode CD8.

Seibler et al teach a rec element, plasmid pOG44, encoding flp recombinase activity (e.g. page 1741, *(d) Recombination Prior to Integration*). Seibler et al teach a first integration cassette, a first target cassette and a rec element. Seibler et al teach a first integration cassette (P construct) comprising an FTR site interposed between an SV40 promoter and a bicistronic expression unit consisting of the SEAP and HygTk genes followed by a second FRT site different from the first FRT site (e.g. Figure 2; paragraph bridging pages 1742-1743). The first integration cassette is capable of random integration into the genome of a cell (e.g. page 1741, *Transfection (Stable Expression)*). Seibler et al teach a first target cassette (promoter-free exchange plasmid) comprising a bicistronic expression unit, consisting of the luciferase and puromycin resistance genes, flanked by FRT sites capable of recombining with the first and second FRT sites of the first integration vector (e.g. Figure 2; paragraph bridging pages 1742-1743). Seibler et al tech the use of a Flp recombinase activity in mammalian cells (e.g. Table 1; Figure 1; page 1741, *(d) Recombination Prior to Integration*; Figure 3). Seibler et al teach that mammalian cells are capable of supporting recombinase mediated cassette exchange (RMCE), which will provide advantages including the ability to create reference integration sites characterized by their expression potential and long-term stability (e.g. page 1747, left column).

Mazda et al teach nucleic acid constructs comprising the murine CD8α gene cDNA, which is used as a reporter/marker gene (e.g. Abstract; Figure 1). Mazda et al teach that the advantages of using CD8 as a reporter or marker is that the assay for CD8 expression is rapid and

easy to perform—cell lysates do not need to be prepared and radioisotopes are not required (e.g. paragraph bridging pages 59-60). Further, the use of CD8 allows other reporter and control genes to analyzed simultaneously if desired (e.g. paragraph bridging pages 59-60). CD8 expression can be analyzed at the single cell level, while the cell remains viable, and the expression is highly reproducible (e.g. page 60).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Cheo et al with regard to the cellular expression system capable of performing site-specific recombinase mediated cassette exchange to include the rec element encoding flp recombinase taught by Seibler et al because Cheo et al teach it is within the ordinary skill in the art to perform recombination reactions *in vivo* in mammalian cells and Seibler et al teach the use of flp recombinase activity encoded by a plasmid to mediate site-specific recombination reactions *in vivo* in mammalian cells. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the hCD4 reporter taught by Ogilvy et al in the integration cassette of Cheo et al, because Cheo et al teach the inclusion of phenotypic markers such as cell surface proteins, and Mazda et al teach the use of murine CD8 as a cell surface reporter.

One would have been motivated to make such a modification in order to receive the expected benefit of identifying reference integration sites in the mammalian genome for reproducible levels of expression as taught by Seibler et al. Further, one would have been motivated to use the CD8 reporter of Mazda et al because it allows cell-by-cell analysis, while the cells remain viable, and the assay is rapid and easy to perform. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to

the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 66-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheo et al (US Patent Application Publication No. 2002/0007051, cited in a prior action; see the entire reference) in view of Seibler et al (Biochemistry, Vol. 36, pages 1740-1747, 1997, cited in a prior action; see the entire reference), Ow (US Patent Application Publication No. 2002/0123145, cited in a prior action; see the entire reference), and Mazda et al (Journal of Immunological Methods, Vol. 169, pages 53-61, 1994; see the entire reference). This is a new rejection, necessitated by the amendment of claim 66 to limit the first scorable homeostatic reporter element to one that comprises a scorable reporter gene encoding CD8, in the reply filed 2/15/2007.

The teachings of Cheo et al are described above and applied as before.

Cheo et al do not teach a rec element encoding at least one flp recombinase activity that recognizes the recombinase recognition sites of the first integration cassette and second integration cassette. Cheo et al do not teach the use of maker genes that encode CD8. Cheo et al do not teach the inclusion of the rec element in the first integration cassette or the first target cassette.

Seibler et al teach a rec element, plasmid pOG44, encoding flp recombinase activity (e.g. page 1741, *(d) Recombination Prior to Integration*). Seibler et al teach a first integration cassette, a first target cassette and a rec element. Seibler et al teach a first integration cassette (P construct) comprising an FTR site interposed between an SV40 promoter and a bicistronic

expression unit consisting of the SEAP and HygTk genes followed by a second FRT site different from the first FRT site (e.g. Figure 2; paragraph bridging pages 1742-1743). The first integration cassette is capable of random integration into the genome of a cell (e.g. page 1741, *Transfection (Stable Expression)*). Seibler et al teach a first target cassette (promoter-free exchange plasmid) comprising a bicistronic expression unit, consisting of the luciferase and puromycin resistance genes, flanked by FRT sites capable of recombining with the first and second FRT sites of the first integration vector (e.g. Figure 2; paragraph bridging pages 1742-1743). Seibler et al tech the use of a Flp recombinase activity in mammalian cells (e.g. Table 1; Figure 1; page 1741, *(d) Recombination Prior to Integration*; Figure 3). Seibler et al teach that mammalian cells are capable of supporting recombinase mediated cassette exchange (RMCE), which will provide advantages including the ability to create reference integration sites characterized by their expression potential and long-term stability (e.g. page 1747, left column).

Ow teaches a first integration cassette, first target cassette and rec element. Ow teaches a first integration cassette (receptor construct) comprising a promoter operably linked to a first exchangeable reporter segment comprising a thymidine kinase (tk) coding region and a zeocin resistance coding region, wherein the tk coding sequence is linked to a first recombinase recognition site (PP') at its 5' end and to a second recombinase recognition site at its 3' end (PP') (e.g. Figure 4). More generally, Ow teaches integration cassettes comprising a polynucleotide flanked by two irreversible recombination sites (IRSs), which are stably integrated into the genome of a host organism (e.g. paragraphs [0014] and [0042]). Because the cassettes do not comprise sequence homologous to a chromosome of the target organism, integration will be random. Ow teaches a first target cassette (donor construct) comprising a third recombinase

recognition site (BB'), capable of recognizing the first recognition site in the first integration cassette; a first target element (cDNA); and a fourth recombinase recognition site (BB'), capable of recognizing the second recombinase recognition site in the first integration cassette (e.g. Figure 4). More generally, Ow teaches target cassettes comprising a polynucleotide flanked by two irreversible complementary recombination sites (CIRSs) (e.g. paragraphs [0014] and [0042]). Ow teaches a rec element encoding a recombinase polypeptide capable of catalyzing a recombination reaction between IRS and CIRS, wherein introduction of the rec element and the first target cassette to the recombinant cell population comprising the first integration cassette results in site-specific substitution of the first exchangeable reporter segment with the first exchangeable target segment (e.g. Figure 4, paragraphs [0014], [0037] and [0054]). Ow teaches that the rec element (polynucleotide encoding the recombinase) can be included in the first integration cassette (receptor construct) containing the IRSs (e.g. paragraphs [0045] and [0054]). Ow teaches that the rec element can be included in the first target cassette (donor construct) containing the CIRSs (e.g. paragraph [0054]). Ow teaches the use of the abovementioned system in host cells such as mammalian cells, fungi and bacteria. Ow teaches a first target element further comprising a first target gene and a first selectable marker gene (e.g. paragraphs [0060] and [0180]).

Mazda et al teach nucleic acid constructs comprising the murine CD8α gene cDNA, which is used as a reporter/marker gene (e.g. Abstract; Figure 1). Mazda et al teach that the advantages of using CD8 as a reporter or marker is that the assay for CD8 expression is rapid and easy to perform—cell lysates do not need to be prepared and radioisotopes are not required (e.g. paragraph bridging pages 59-60). Further, the use of CD8 allows other reporter and control

genes to analyzed simultaneously if desired (e.g. paragraph bridging pages 59-60). CD8 expression can be analyzed at the single cell level, while the cell remains viable, and the expression is highly reproducible (e.g. page 60).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Cheo et al with regard to the cellular expression system capable of performing site-specific recombinase mediated cassette exchange to include the rec element encoding flp recombinase taught by Seibler et al because Cheo et al teach it is within the ordinary skill in the art to perform recombination reactions *in vivo* in mammalian cells and Seibler et al teach the use of flp recombinase activity encoded by a plasmid to mediate site-specific recombination reactions *in vivo* in mammalian cells. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the rec element in the first integration cassette or first target cassette, because Cheo et al and Ow et al teach is it within the skill of the art to use recombinase activity to perform site specific recombination and exchange of nucleic acid segments. Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the hCD4 reporter taught by Ogilvy et al in the integration cassette of Cheo et al, because Cheo et al teach the inclusion of phenotypic markers such as cell surface proteins, and Mazda et al teach the use of murine CD8 as a cell surface reporter.

One would have been motivated to make such a modification in order to receive the expected benefit of identifying reference integration sites in the mammalian genome for reproducible levels of expression as taught by Seibler et al. Further, one would have been motivated to include the rec element in either the first integration cassette or first target cassette

in order to receive the expected benefit of having a system where fewer nucleic acid molecules need to be introduced into the cell in order to support the desired recombination method. Moreover, one would have been motivated to use the CD8 reporter of Mazda et al because it allows cell-by-cell analysis, while the cells remain viable, and the assay is rapid and easy to perform. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments - 35 USC § 103

The rejection of claims 66 and 70-83 under 35 U.S.C. 103(a) as being unpatentable over Cheo et al in view of Seibler et al has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/15/2007. The references do not teach a scorable reporter gene encoding CD8.

The rejection of claims 66 and 70-83 under 35 U.S.C. 103(a) as being unpatentable over Cheo et al in view of Cox et al has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/15/2007. The references do not teach a scorable reporter gene encoding CD8.

The rejection of claims 66-68 and 70-83 under 5 U.S.C. 103(a) as being unpatentable over Cheo et al in view of Seibler et al and Ow has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/15/2007. The references do not teach a scorable reporter gene encoding CD8.

The rejection of claims 66 and 69-83 under 35 U.S.C. 103(a) as being unpatentable over Cheo et al in view of Seibler et al and Ogilvy et al has been withdrawn in view of Applicant's amendment to the claims in the reply filed 2/15/2007. The references do not teach a scorable reporter gene encoding CD8.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached at 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

jad

CELINE QIAN, PH.D.
PRIMARY EXAMINER